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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,700	03/13/2002	Edwin L. Madison	24745-1613	4309

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/099,700	MADISON ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,8-10,18,19,50-55,59-61,65-67 and 69-122* is/are pending in the application.

4a) Of the above claim(s) *73-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,9,10,18,19,50-55,59-61,65-67,69-72 and 117-122* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/29/04 7 6/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's Amendment filed June 17, 2004, has been entered and it is agreed that amendments to paragraphs at pages 9, 19, 20, 43, 54, 75, 79, and 158 of the specification add no new matter because they correct obvious errors. The amendment to paragraph 158 overcomes the objection of record to the specification. The amendment of June 17, 2004, also amends the elected claims 1, 2, 4, 6, 52 and 69, cancels claims 3, 7, 11-17, 20-49, 56-58, 62-64 and 68 and adds new claims 117-122. Non-elected claims 73-116 remain in the application, of which claims 78, 85, 91, 97, 101, 106, and 111 are amended. In the event of rejoinder, any rejoined process claim must meet the requirements of 35 U.S.C. §§ 101, 102, 103, and 112 even though the restriction requirement between the product claims and non-elected process claims be withdrawn. The amendments to the elected claims, together with the claim cancellations, overcome rejections of record of several of the elected claims herein under the second paragraph of 35 U.S.C. § 112. Claims 1, 2, 4-6, 8-10, 18, 19, 50-55, 59-61, 65-67, and 69-122 are now pending herein and claims 73-116 are withdrawn from consideration as drawn to non-elected inventions.

Information Disclosure Statements

The information disclosure statements (IDS) submitted January 29, and June 16, 2004, thus filed after the communication on the merits mailed December 17, 2003, are in compliance with the provisions of 37 CFR 1.97. Accordingly, they were considered by the examiner and executed copies of the PTO-Forms 1449 that accompanied both submissions are included in this communication.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 65-67 and 69-72 remain rejected for reasons of record under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

Applicant's arguments filed June 17, 2004, have been fully considered but are not persuasive in establishing that any "modulator" of a disclosed MTSP7 protease has a specific and substantial utility. As Applicant notes, it was agreed previously that a native MTSP7 protease applicant discloses has a specific and substantial utility because it can cleave a specific, artificial, tripeptide substrate, S-2366, a utility present in at least one embodiment of the product claims 1 and 4 from which claims 65-67 and 69-72 depend: a protease that comprises a portion of the native MTSP7 serine protease of SEQ ID NO:16, which portion comprises the catalytic domain of SEQ ID NO:18.

Applicant urges at pages 21-25 of the Response filed June 17, 2004, that this *in vitro* utility of the protease ensures that any "modulator" will have utility as well, specifically as "diagnostic reagents to detect MTSP7" and as "therapeutic candidates". But the latter proposed utility for a product that might be found by practicing a method of the claims rejected herein is characterized by Applicant at the close of page 23 of the Response as that of "potential therapeutics[, t]hus, [claimed] methods of identifying modulators provide potential candidates for . . . potential treatments". The instant application identifies no specific utility for a modulator identified by methods of claims 65-64 and 69-72, and the Response alleges only a "potential" rather than a substantial utility for such a modulator, to treat no particular disease or medical condition known to the inventors at the time the application was filed. Applicant also fails to establish that a product found by practicing a claimed method can have any substantial and specific affect on the protease itself because the public cannot know how to use modulators

identified by a claimed assay to achieve a specific or substantial alteration of the unknown, native, proteolytic activity of the disclosed MTSP7 protease.

With respect to a proposed diagnostic utility for a modulator found by a method of the rejected claims, Applicant's argument is not based on a limitation present in the rejected claims. Applicant did not elect for prosecution claims drawn to methods for identifying molecules that might bind to a MTSP7 protease and claims 65-72 rejected herein do not require "binding" by a modulator detected by their recited methods. Where the specification does not identify, and Applicant's response does not point to, any specific disease or medical condition for potential diagnosis, an argument for "diagnostic" utility begs the question of what, specifically, is to be diagnosed? It is clear that a modulator produced by a claimed method could only be used in a context already found by the Supreme Court to be unpatentable: "use of a material for further research to determine, e.g., its specific . . . role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). There is no disclosure in the specification that suggests Applicant knew of any specific utility for a modulator that might be identified by a claimed method that would permit its use, tolled by the filing date of the instant application, by the public in any specific or substantial fashion thus the rejection of record is sustained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-72 also remain rejected for reasons of record under 35 U.S.C. § 112, first paragraph, for lack of enablement as to use.

Applicant does not separately argue that the rejection of claims 65-72 under 35 U.S.C. § 112, first paragraph, for lack of enablement as to use fails because it is based on an improper rejection for lack of patentable utility made in the rejection of record of the same claims under 35 U.S.C. § 101. This is considered to be an acknowledgment that the rejections of record of claims 65-72 for lack of utility under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, for lack of enablement stand or fall together, and it is agreed that they do. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1, 2, 4-6, 9, 10, 18, 19, 50-55, 59-61, 65-67 and 69-72 remain rejected for reasons of record, and new claims 117-122 are now rejected, under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed June 17, 2004, have been fully considered but are not persuasive in establishing that the claims as amended on June 17, 2004, state subject matters for which the specification provides an adequate written description where claim 1, as amended, and new claims 119 and 121 allow polypeptides of clause (a) to differ from the sequence of amino acid set forth in SEQ ID NO:18 at as many as 44 amino acid positions, all but one of which are unspecified by either the claims and specification, and also allows polypeptides of clause (b) of the claim to differ at any position in any "sequence of amino acid sequence encoded by . . . SEQ ID NO:15", which may be less than the entire amino acid sequence of SEQ ID NO:16. Similarly, claims 4 and 6 as amended permit a "portion" of a "portion" of a protease in clause (b) of claim 4, and the new claims 117, 118, 120 and 122 also permit, a protease domain to diverge at as many as 23 amino acid positions from the amino acid sequence set forth in SEQ ID NO:16, only one of which is specified by either the claims or the specification. Applicant's arguments are not persuasive because they do not show that the

specification, exemplifies, describes, suggests, or otherwise discusses, the preparation of subject matters of divergent proteases of claims 1, 2, 4-6, 9, 10, 18, 19, and 117-122, or conjugates or solid supports or arrays comprising such proteases of claims 52-55 and 59-61, or methods using such proteases of claims 65-67 and 69-72, wherein generic proteases may differ at as many as 10% of the positions in the amino acid sequence of the protease catalytic domain having the 231-amino acid of SEQ ID NO:18 or in the integral protease of SEQ ID NO:18.

Applicant urges at pages 20-40 of the response filed June 17, 2004, that identifying the catalytic triad of amino acids within the protease domain set forth in SEQ ID NO:18 furnishes adequate identifying characteristics of proteases that may diverge anywhere else among the remaining 228 positions so long as only 23 amino acid positions are altered within the sequence of SEQ ID NO:18. Yet Applicant discusses only the catalytic triad and the cysteine at position 233 of SEQ ID NO:16, which falls within the protease domain, and does not point to where the specification identifies any amino acid sequence features outside the protease domain that might be altered. Alteration of any of the three positions in the catalytic triad will abolish the protease's activity and Applicant cannot point to any teaching in the specification, save for substitution of the cysteine at position 233 of SEQ NO:16, which describes where modifications supporting the functional limitations of the rejected claims should be made. Thus, neither the artisan nor the public reading the claims can know what further amino acid sequence alterations are contemplated by the rejected claims – where they might occur nor what any alteration might be – because the specification does not otherwise disclose or suggest the nature or source of any of the generic proteins of the rejected claims. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v.*

Revel v. Sugano, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). It is agreed that Applicant identifies a substrate with which to assay the proteolytic activity of an altered structure but the specification fails to show that Applicant had identified those structural features of the protease that permit recognition of the substrate, thus one of skill in the art would not recognize Applicant's possession of divergent polypeptides differing significantly, at 90% of the positions, from the protease domain of SEQ ID NO:16, yet functioning as proteases with a single disclosed substrate where the specification leaves the task of determining the location and the nature of any alterations beyond a substitution for the cysteine at position 212 of SEQ ID NO:18 to the subsequent experimentation of others.

The identifying characteristics the specification identifies, just four amino acid sequence positions in the protease domain, constitute less than 2% of the 231 amino acid positions within that domain. In addressing the issue of whether a disclosure of a molecular structure of a single species of polypeptide could adequately describe the molecular structure of a functionally similar molecular species, the Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of any undisclosed generic protease to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The rejection of record is maintained because the specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could

not predict the structure, or other properties, of the generic proteases of claims 4, 6, 11, and 111-114, or the conjugates of claims 52-55 comprising such proteases.

Claims 1, 2, 4-6, 9, 10, 18, 19, 50-55, 59-61, 65-67 and 68-72 remain rejected for reasons of record under 35 U.S.C. § 112, first paragraph, because while the specification is enabling for,

(i) a polypeptide capable of cleaving the artificial substrate S-2366, which may be a fusion polypeptide, comprising the MTSP7 protease catalytic domain having the amino acid sequence of SEQ ID NO:18,

(ii) a protease capable of cleaving the artificial substrate S-2366 comprising the amino acid sequence set forth in SEQ ID NO:16 as well as its activated two-chain form,

(iii) a protease capable of cleaving the artificial substrate S-2366 consisting of the MTSP7 protease catalytic domain with the amino acid sequence set forth in SEQ ID NO:18,

(v) a variant of proteases of clauses (i)-(iii) wherein a free cysteine in the protease domain is replaced with another amino acid, such as serine, and,

(vi) conjugates comprising same, solid supports attached to same, and assay methods utilizing same,

is not enabling for any embodiment of a polypeptide comprising a MTSP7 protease catalytic domain having an amino acid sequence diverging from the amino acid sequence or SEQ ID NO:18 at as many as 23 amino acid positions or a polypeptide comprising a MTSP7 protease having an amino acid sequence diverging from the amino acid sequence or SEQ ID NO:16 at as many as 44 amino acid positions, nor for conjugates comprising same, solid supports attached to same, and methods of screening for modulators of protease activity comprising same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed June 17, 2004, have been fully considered but are not persuasive in establishing that the claims as amended on June 17, 2004, state subject matters enabled by guidance present in the specification as filed, even if combined with teachings provided in the prior art of record herein. The rejection statement above is modified in view of the amendments of June 17, 2004, but Applicant's arguments filed June 17, 2004, do not show where or how the specification supports arbitrary allocations throughout the amino acid sequence of SEQ ID NO:16 of amino acid substitutions, additions, or deletions at as many as 44 positions therein, or the arbitrary allocations throughout the amino acid sequence of SEQ ID NO:18 of amino acid

substitutions, additions, or deletions at as many as 23 positions therein, permitted by the rejected claims.

At pages 40-54 of the Response filed June 14, 2004, Applicant urges that knowledge of structures of other mammalian Type II serine proteases can replace the need for any guidance in the specification as to where to chose 23 amino acid positions for alteration in the MTSP7 catalytic domain amino acid sequence of SEQ ID NO:18, or where to chose 44 amino acid positions for alteration in the integral MTSP7 amino acid sequence of SEQ ID NO:16. At page 51 of the Response, Applicant cites Alsobrook et al., of record, for the proposition that "up to about 54% changes in the amino acid sequence" of their NOV1 protease can be made "and retain catalytic activity" but Alsobrook et al. are just as silent as the instant specification as to where to make any change and what the change should be. Also at page 51 of the Response, Applicant cites Bryan et al.. made of record with Applicant's Information Disclosure Statement, for the proposition that "the serine protease subtilisin can tolerate mutations in up to 50% of its amino acid residues" without compromising structural and functional characteristics. But Bryan et al. are not discussing concurrent alterations of a bacterial serine protease not closely related to the mammalian Type II serine proteases, the crystal structure of which was determined over 25 years ago and which has been the subject of many foreign and domestic patent application filings, demonstrating but incremental progress through the intervening decades in identifying specific positions for alterations, usually quite specific alterations, none of which yet disclose a concurrent set of alterations at as many as 6% of the 275 amino acid positions in the sequence of the mature protease.

By contrast, Applicant reiterates the limited teachings of the specification identifying the three positions of the amino acid sequences of SEQ IDs NOs:16 and 18, the catalytic triad in the protease domain, that are best left unchanged, identifying a proposed activation cleavage site, and identifying a cysteine in the amino acid

sequence of SEQ ID NO:16, but points to no prior art teachings demonstrating that anyone had succeeded in making alterations as extensive as those embraced by the claims within a mammalian Type II serine protease domain, whether or not a functional protease resulted. Most importantly, Applicant cannot point to any teaching in the specification of the nature of such extensive alterations that might result in a variant to that will function as a protease. The specification, even if combined with the state of art evidenced by the prior art made of record herewith, does not support the introduction of a 10% divergence in the amino acid sequence of the catalytic domain set forth in SEQ ID NO:18 where the prior art made of record herewith does not, taken together, identify even a few positions among the amino acid sequences of catalytic domains of the human proteases matripase, PSA, and hepsin, cited in the specification, that can be altered yet permit retention of catalytic activity with the artificial peptide substrate disclosed in the specification or retention of the undisclosed, native, proteolytic activity of an MTSP7 protease having the amino acid sequence of SEQ ID NO:16.

Undirected perturbation of an amino acid sequence cannot enable the design and preparation of the myriad of divergent proteases embraced by the claims yet provide the public with a divergent protease that will retain its native activity. It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in

the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); **see also**, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure of a single B-cell growth factor allele). The Federal Circuit approved the standard set by the CCPA in *Fisher* in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Applying factors discussed in the enablement analysis in *Wands*, ***supra***, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of the MTSP7 protease catalytic domain set forth in SEQ ID NO:18 to the extent permitted by the rejected claims,

b) the specification lacks working examples wherein the MTSP7 protease catalytic domain set forth in SEQ ID NO:18 is altered to the extent permitted by the rejected claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class of human serine proteases having domains that correspond to the MTSP7 protease catalytic domain set forth in SEQ ID NO:18 have had as many as 23 amino acids specifically identified for concurrent modification.

The rejection of record is maintained because the scope of subject matters embraced by the limitation, "90% sequence identity", is unsupported by the present specification even when taken in combination with the teachings of the prior art of record herein.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, 52-55, 69, 117 and 118 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments at pages 61-63 of the Response filed June 17, 2004, together with the claim amendments submitted therewith overcome, the greater part of

the claim rejections of record under the second paragraph of 35 U.S.C. § 112, including the rejections of record of claims 6, 52-55 and 69. Claims 6, 52-55 and 69, and the new claims 117 and 118 however, are subject to a new ground of rejection necessitated by the amendment of claim 4 filed June 17, 2004, from which they depend. With the entry of Applicant's amendment filed June 14, 2004, claims 4, 6, 52-55, 69, 117 and 118 remain indefinite because claim 4 ambiguously recites,

"A . . . polypeptide, wherein:

the MTSP7 **portion** of the polypeptide consists essentially of the protease domain of the MTSP7 or a catalytically active **portion** thereof;

the protease domain of the MTSP7 or the catalytically active **portion** thereof is selected from the group consisting of"

(emphases supplied) where the recitation at lines 3 and 4 of the claim cannot establish what any "MTSP7 portion" might "consist[ ] essentially of" in stating not one, but two, options where the second option is, again, a "portion". The next phrase at lines 5 and 6 of the claim also fails to define that which is a portion of a portion in reciting "the protease domain or . . . portion thereof is selected from the group consisting of". Claims 6, 52-55, 69, 117 and 118 are included in this rejection because they depend from claim 4 but do not otherwise resolve its indefinite description.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language.

Claims 4 and 6 remain rejected for reasons of record, and claims 52-55 and 69 as well as the new claims 120 and 122 are now rejected, under 35 U.S.C. § 102(e)(1) as being anticipated by Alsobrook et al., US 2003/0170630, of record.

Applicant's arguments filed June 14, 2004, have been fully considered but are not persuasive in establishing that the amended claims 4 and 6 avoid the disclosure of Alsobrook et al. of their human serine protease of SEQ ID NO:2 comprising a 420-amino acid sequence wherein an "MTSP7 portion" is identical to the amino acid sequence of SEQ ID NO:18 herein meeting structural limitations of clause (b) of claim 4, and claim 6 dependent thereon. Claims 120 and 122 are now included in this rejection because the disclosure of Alsobrook meets their structural limitations in paragraphs 410, 520-524 and 528-531 where recombinant expression of the protease in eukaryotic host cells will inherently result in an activation cleavage. Alsobrook et al. need disclose no further protease or conditions for such an activation cleavage where the instant specification fails to disclose either an activating protease, or conditions for activation, of a MTSP7 protease as a two-chain protease. Applicant's amendment of claim 4 and concomitant amendments to claim 52, 54 and 69 of June 14, 2004, that make these depend ultimately from claim 4 necessitate inclusion of claims 52-55 and 69 in this rejection where Alsobrook et al. also disclose the preparation of conjugates comprising targeting agents linked to any of their disclosed proteins so as to permit attachment of the conjugate to a surface and its subsequent detection in paragraph 576, meeting limitations of claims 52-55, and methods for using their disclosed proteins to screen test compounds to detect modulators of the activity of the proteins in paragraphs 18, 19, 563, and 577. Thus the rejection of record is maintained and is extended to claims 52-55, 120 and 122 as necessitated by Applicant's amendments.

Conclusion

Claim 8 remains objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
September 3, 2004

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600